PB88-131081

Health and Environmental Effects Profile for Trinitrophenols

(U.S.) Environmental Protection Agency
Cincinnati, OH

Jan 84

U.S. Department of Commerce
National Technical Information Service
NTIS

TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)	
1. REPORT NO. EPA-600/X-84-141	2.
3. RECIPIENT'S ACCESSION NO. PB88 131081/AS	
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Trinitrophenols	5. REPORT DATE January 1984
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268	13. TYPE OF REPORT AND PERIOD COVERED
	14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES	

16. ABSTRACT

The Health and Environmental Effects Profile for trinitrophenols was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for trinitrophenols.

17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field Group
18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 42
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PB88-131081

EPA/600/X-84/141
January 1984

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR TRINITROPHENOLS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA. 22161

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	2
1.3.	PRODUCTION DATA	3
1.4.	USE DATA	3
2.	ENVIRONMENTAL FATE AND TRANSPORT PROCESSES	5
2.1.	AIR	5
2.2.	WATER	5
2.3.	SOIL	6
3.	EXPOSURE	9
4.	PHARMACOKINETICS	10
4.1.	ABSORPTION	1
4.2.	DISTRIBUTION	10
4.3.	METABOLISM	11
4.4.	EXCRETION	11
5.	EFFECTS	12
5.1.	CARCINOGENICITY	12
5.2.	MUTAGENICITY	12
5.3.	TERATOGENICITY	15
5.4.	OTHER REPRODUCTIVE EFFECTS	15
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	16
5.6.	OTHER RELEVANT INFORMATION	16
6.	AQUATIC TOXICITY	18
6.1.	ACUTE TOXICITY	18
6.2.	CHRONIC TOXICITY	19
6.3.	PLANT EFFECTS	19
6.4.	RESIDUE	19
6.5.	OTHER RELEVANT INFORMATION	19
7.	EXISTING GUIDELINES AND STANDARDS	20
7.1.	HUMAN	20
7.2.	AQUATIC	20
8.	RISK ASSESSMENT	21
9.	REFERENCES	23
APPENDIX:	LITERATURE SEARCHED	34

LIST OF ABBREVIATIONS

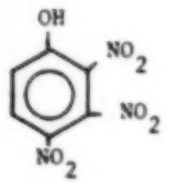
ADI	Acceptable daily intake
BOD	Biochemical oxygen demand
COD	Chemical oxygen demand
LC_{50}	Concentration lethal to 50% of recipients
LD_{Lo}	Lowest lethal dose
NAD	Nicotinamide adenine dinucleotide
NOEL	No-observed-effect level
ppm	Parts per million
s.c.	Subcutaneous
STEL	Short-term exposure limit
TLV-TWA	Threshold limit value-Time-weighted average

1. INTRODUCTION

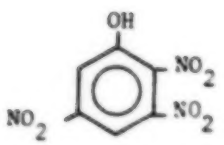
1.1. STRUCTURE AND CAS NUMBER

The common name for 2,4,6-trinitrophenol is picric acid. This compound is also known as CI 10305, melinite, picral, carbazotic acid, nitroxanthic acid, 2-hydroxy-1,3,5-trinitrobenzene, phenol trinitrate and picronitric acid (NIOSH, 1983). No synonyms were found for 2,3,4-, 2,3,5-, 2,3,6- or 3,4,5-trinitrophenol. The molecular formula of the trinitrophenol isomers is $C_6H_3N_3O_7$ and the molecular weight is 229.11 (Windholz, 1976). The structures of the trinitrophenols are given below:

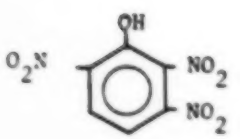
2,3,4-trinitrophenol



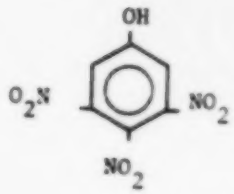
2,3,5-trinitrophenol



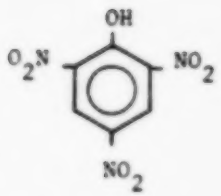
2,3,6-trinitrophenol



3,4,5-trinitrophenol



2,4,6-trinitrophenol



The Chemical Abstracts Service (CAS) Registry Number for 2,4,6-trinitrophenol is 88-89-1; no CAS numbers were found for the remaining trinitrophenol isomers.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

2,4,6-Trinitrophenol exists as pale yellow, odorless, intensely bitter crystals (Windholz, 1976). Some of the physical properties of 2,4,6-trinitrophenol are given below:

Specific gravity at 20°C:	1.763 (von Oettingen, 1941)
Boiling point:	Explodes at >300°C (U.S. EPA/NIH, 1983)
Melting point:	122-123°C (Windholz, 1976)
Solubility in water at 25°C:	14,000 mg/ℓ (U.S. EPA/NIH, 1983)
Vapor pressure:	2 mm Hg at 195°C; 50 mm Hg at 255°C (U.S. EPA/NIH, 1983)
Flash point:	150°C (U.S. EPA/NIH, 1983)
Auto ignition point:	300°C (U.S. EPA/NIH, 1983)

2,3,5-Trinitrophenol forms yellow, needle-shaped crystals, has a melting point of 119-120°C and is soluble in acetic acid, alcohol and benzene (von Oettingen, 1941).

2,3,6-Trinitrophenol forms white, needle-shaped crystals, has a melting point of 117-118°C, is soluble in hot water (quantitative data not specified) and is very soluble in alcohol and ether (von Oettingen, 1941).

In addition to the trinitrophenol isomers that are the subject of this document, another isomer, 2,4,5-trinitrophenol, forms white, needle-shaped crystals, has a melting point of 96°C, is soluble in hot water (quantitative data not specified) and is very soluble in alcohol and water (von Oettingen, 1941).

Physical and chemical properties of 2,3,4- and 3,4,5-trinitrophenol were not available.

1.3. PRODUCTION DATA

2,4,6-Trinitrophenol is prepared by sulfonating phenol and then treating the reaction mixture with nitric acid, or by treating benzene with nitric acid and mercuric nitrate, or by nitration of 2-tert-butyl-4,6-dinitrophenol (Windholz, 1976). 2,4,6-Trinitrophenol is manufactured by American Research Products, Co., South Euclid, OH; Martin Marietta Corp., Charlotte, NC; and Hummel Chemical Co., South Plainfield, NJ (U.S. EPA/NIH, 1983; U.S. EPA, 1983). No production volumes were available for any of the manufacturers (U.S. EPA, 1983). 2,4,6-Trinitrophenol is also imported by Henley and Co., Inc., New York, NY (U.S. EPA/NIH, 1983).

1.4. USE DATA

Currently, the major commercial use of 2,4,6-trinitrophenol is in the synthesis of dye intermediates, especially the sodium salt of picramic acid (2-amino-4,6-dinitrophenol). 2,4,6-Trinitrophenol is also used to manufacture picrates; ammonium picrate, sodium picrate and potassium picrate are made on a small commercial scale, up to 1000 pounds annually. 2,4,6-Trinitrophenol was used as an explosive until it was displaced by trinitro-

toluene and more superior explosives; current specialty uses of 2,4,6-trinitrophenol in explosives are few. 2,4,6-Trinitrophenol has been used as a germicide, as a fungicide, in tanning agents, as an analytical reagent, in photochemicals, as a pharmaceutical burn antiseptic, as an intermediate for making specialty medicinals, as a process material for etching metals, in matches, fireworks and pyrotechnics, and in electric batteries; these applications are currently judged to be minor uses (Matsugma, 1967; Hawley, 1977).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

There are only limited data on the fate and transport of 2,4,6-trinitrophenol in air. Based on its high water solubility of 14,000 mg/ℓ (U.S. EPA/NIH, 1983), low vapor pressure (U.S. EPA/NIH, 1983) and evidence of its adsorption to at least one soil type (Nose et al., 1964), it is unlikely that 2,4,6-trinitrophenol will volatilize significantly from water or soil into the atmosphere.

2.1. AIR

The fate of 2,4,6-trinitrophenol in the atmosphere will depend upon its reactivity with O_3, NO_x and free radicals (e.g., RO•, O•, RO_2•) and its ability to undergo photolysis. Gold and Rochester (1964) exposed methanolic solutions of 2,4,6-trinitrophenol and sodium methoxide to irradiation with visible light. This irradiation was reported to cause or accelerate cleavage of a nitro group; however, it is unlikely that such a reaction will take place in the ambient atmosphere in the absence of appropriate methoxide concentration.

2.2. WATER

Due to its high water solubility, 2,4,6-trinitrophenol may enter the aquatic media through runoff and leaching from soil. The plausible mechanisms for removal of 2,4,6-trinitrophenol from water include photochemical reaction, hydrolytic reaction and microbial degradation. The study by Gold and Rochester (1964) indicates that 2,4,6-trinitrophenol has the potential for photolysis, and studies in soil indicate that microbial degradation may be a significant process for removal of 2,4,6-trinitrophenol from water; however, there are neither specific studies regarding these two processes in water nor studies defining hydrolysis of 2,4,6-trinitrophenol in water.

2.3. SOIL

The fate and transport of 2,4,6-trinitrophenol has been studied most extensively in soil. McKee and Wolf (1963) reported that passage of 2,4,6-trinitrophenol through soil does not appear to neutralize or remove the compound. The two potential processes that may control the transport of 2,4,6-trinitrophenol in soils are volatilization and leaching. The volatilization of 2,4,6-trinitrophenol from soils is likely to be an insignificant process because of its high water solubility. 2,4,6-Trinitrophenol appears to be leached from some soil types, as the compound was detected in a well located ~1 mile from a defunct plant that had manufactured explosives (Cole, 1974). Based on the reported water solubility of 14,000 mg/ℓ, the log octanol-water partition coefficient (log K_{ow}) of 2.03 (Hansch and Leo, 1979) and the regression equations of Kenaga and Goring (1980), a soil adsorption coefficient in the range of 23-303 is predicted for 2,4,6-trichlorophenol. This range indicates a moderate potential for mobility in soils, especially in soils of low organic content. Nose et al. (1964) reported that adsorption of 2,4,6-trinitrophenol to fuller's earth increased as the pH was lowered from 4 to 2.

Goodwin et al. (1977) measured the COD of 2,4,6-trinitrophenol and found that 100% had completely oxidized after 120 minutes. Ryerman et al. (1966) reported a 1-day BOD of <1 pound of O_2 consumed/pound of 2,4,6-trinitrophenol. These laboratory tests indicate that 2,4,6-trinitrophenol may be biologically oxidized under certain conditions, which may or may not be applicable to natural systems.

Available data indicate that some microorganisms may biodegrade 2,4,6-trinitrophenol in soil. 2,4,6-Trinitrophenol is slightly degraded

(<2%) to picramic acid and other unidentified amino derivatives via reduction of the nitro groups by Pseudomonas which used this compound as the sole source of carbon (Wyman et al., 1979; Gvozdyak et al., 1974, Won, 1977; Brebion et al., 1967). No detectable degradation of a 0.1% solution of 2,4,6-trinitrophenol was accomplished by mixed cultures from soil, compost, activated sewage sludge, or estuarine sediment under anaerobic or aerobic conditions for 3 months (Wyman et al., 1979). 2,4,6-Trinitrophenol, serving as the sole source of carbon for the microbes, resisted degradation by adapted activated sludge (Pitter, 1976; Pitter et al., 1974).

Tsukamura (1954a,b, 1960) reported that both whole cells and cell-free extracts of Mycobacterium avium reduced 2,4,6-trinitrophenol to picramic acid. The authors suggested that biodegradation is accomplished enzymatically via a reduced NAD-flavoprotein system in M. avium.

A number of soil microorganisms adapted to dinitro-o-cresol were shown to almost completely metabolize the nitro group of 2,4,6-trinitrophenol with the formation of nitrite, which requires cleavage of C-N bonds, suggesting that dinitrophenols may be a metabolic product (Jensen and Lautrup-Larsen, 1967; Gundersen and Jensen, 1956). It is unclear from the results if the microorganisms cause ring cleavage and/or derive any carbon from the compound. One of the organisms in this study was identified as Arthrobacter simplex; other organisms were provisionally referred to as Arthrobacter x and Pseudomonas. The metabolic attack on 2,4,6-trinitrophenol was accompanied by formation of an unidentified soluble rust-brown pigment (structure unknown).

The experimental findings of Chambers et al. (1963) indicate that a phenol-adapted culture was able to slowly oxidize 2,4,6-trinitrophenol. The

results of oxygen uptake studies with nitrophenolic compounds must be interpreted with caution, as the possibility cannot be excluded that the increased oxygen uptake observed by Chambers et al. (1963) was due to the enhancement of endogenous oxygen uptake by 2,4,6-trinitrophenol because of its uncoupling effect.

In a comprehensive review of nitroaromatic compounds, Howard et al. (1976) concluded that 2,4,6-trinitrophenol is susceptible to partial degradation by certain microorganisms. It may be speculated that 2,4,6-trinitrophenol would be subject to microbial attack in the environment by the microorganisms adapted to phenol or the herbicide dinitro-o-cresol. Both phenol and dinitro-o-cresol appear to be widespread contaminants and, thus, the microorganisms adapted to them may also be expected to be widespread.

3. EXPOSURE

STORET contains one listing for 2,4,6-trinitrophenol in May, 1981. The mean concentration found in Niagara River sediment was 31,200 µg/kg.

In 1955, 2,4,6-trinitrophenol was detected at a concentration of 0.7 mg/ℓ in a well located ~1 mile from a plant engaged in the manufacture of explosives from 1914-1918 (Cole, 1974). Harris et al. (1946) reported 2,4,6-trinitrophenol concentrations of 2-20 µg/ℓ in distilled seawater which was used as drinking water on an American ship anchored at Wakayama, Japan. Analysis of the seawater failed to yield detectable levels of 2,4,6-trinitrophenol. The contamination resulted from dumping ammunition containing 2,4,6-trinitrophenol into the water near the ship 3 weeks prior to the analysis.

4. PHARMACOKINETICS

All of the data discussed regarding the absorption, distribution, metabolism and excretion of 2,4,6-trinitrophenol is from early literature [pre-1936, including the review of these data in Williams (1959) and qualitative absorption data from Bruin et al. (1980)]. Therefore, the experimental designs and instrumentation used in these studies might be judged inadequate by present standards. Nevertheless, the data are presented because of the absence of more recent studies.

4.1. ABSORPTION

Absorption of 2,4,6-trinitrophenol can occur by ingestion, inhalation or dermal contact, but quantification studies were not available (Bruin et al., 1980). Dermal absorption by humans following topical application has been reported (Rutledge, 1936; Dennie et al., 1929). Absorption of 2,4,6-trinitrophenol by dogs given the compound via s.c. injection or dermal application was reported by Dennie et al. (1929).

4.2. DISTRIBUTION

Only two studies, both from the earlier literature, were found concerning the distribution of 2,4,6-trinitrophenol. These studies were available only in abstract form and, therefore, lack many details. Guerbet and Mayer (1932) reported finding 2,4,6-trinitrophenol metabolites (picramic acid, glucuronide conjugates and carbamidonitrophenols) in the liver, kidneys, brain, blood and spinal fluid of exposed mammals (species not reported in the abstract). Malmejac (1917) found 2,4,6-trinitrophenol in the blood and cerebrospinal fluid of humans after topical application of salve containing the compound.

4.3. METABOLISM

Several investigators have reported that 2,4,6-trinitrophenol was reduced to picramic acid by both humans and animals following exposure to the parent compound via ingestion or dermal contact (Guerbet and Mayer, 1932; Koizumi, 1914-1915; Walko, 1901; Karplus, 1893; Barral, 1915; Williams, 1959). Other identified metabolites of 2,4,6-trinitrophenol observed in exposed humans include glucuronide conjugates and carbamidonitrophenols (Guerbet and Mayer, 1932). Karplus (1893) reported an increase in urinary ethereal sulfates in humans poisoned by 2,4,6-trinitrophenol (indicating conjugation of the compound with sulfate). Walko (1901), however, did not find a similar increase in rabbits. Williams (1959) also observed other unidentified metabolites, including a red pigment, in humans occupationally exposed to 2,4,6-trinitrophenol.

Perfusion experiments with the liver, kidneys and spleen indicated that the liver was the most active of the three organs in reducing 2,4,6-trinitrophenol to picramic acid (Giorgi, 1924).

4.4. EXCRETION

2,4,6-Trinitrophenol and its metabolites were excreted in the urine of humans and animals following oral or dermal exposures to the parent compound (Giorgi, 1924; Williams, 1959; Guerbet and Mayer, 1932; Dennie et al., 1929). Dennie et al. (1929) observed 2,4,6-trinitrophenol in the urine of dogs within 24 hours of a s.c. injection or dermal application of the compound. Additional details were not provided in the available literature.

Malmejac (1917) attributed the yellow coloring of the human skin following 2,4,6-trinitrophenol poisoning to the excretion of the compound and its derivatives through the skin.

5. EFFECTS

5.1. CARCINOGENICITY

van Esch et al. (1957) administered a dietary concentration of 500 ppm 2,4,6-trinitrophenol, 2,4,6-trinitroaniline (picramide), or hexanitrodiphenylamine to groups of male (number not reported) and female (N = 10) Wistar rats for 2.5 years; 2,4,6-trinitrophenol and 2,4,6-trinitroaniline are in vitro metabolites of hexanitrodiphenylamine. Two groups of control animals were used for comparison, a group of 19 untreated controls from this experiment and a group of 83 untreated controls from a series of different toxicity experiments in the same laboratory. Neither the incidence nor the types of tumors seen in male rats treated with any of the three test compounds differed significantly from control animals. The incidence of mammary tumors (fibroadenomata, adenofibromata and fibromata) in female rats was 100% (10/10) for those treated with hexanitrophenylamine, 50% (4/8) for 2,4,6-trinitroaniline, 40% (4/10) for 2,4,6-trinitrophenol, and 42% (8/19) and 22% (18/83) for each group of control animals. The evidence from this study was not conclusive, because the incidence of mammary tumors in control animals (8/19; 42%) was higher than usually observed (18/83; 22%) and the number of animals/group was small.

5.2. MUTAGENICITY

Genotoxicity of 2,4,6-trinitrophenol has been tested by both in vitro bacterial and Drosophila melanogaster assays, and in vivo Drosophila and NMRI mice assays. These mutagenicity assays are summarized in Table 5-1.

2,4,6-Trinitrophenol was positive in the reverse mutation assay with S. typhimurium only in the presence of a mammalian metabolic activation system (Won, 1977; Wyman et al., 1979; Yoshikawa et al., 1976; Gocke et al., 1981; Chiu et al., 1978). Picramic acid, an in vivo and in vitro metabolite of

TABLE 5-1

Mutagenicity Testing of 2,4,6-Trinitrophenol (Picric Acid)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Source
Reverse mutation	S. typhimurium TA98	NR	NR	±S9	±	Picramic acid, an in vivo and in vitro metabolite of 2,4,6-trinitrophenol, was mutagenic to tester strains TA98, TA100, TA1535 and TA1538 in the absence of a mammalian metabolic activation system. On this basis, Wen (1977) suggested that the metabolite rather than the parent compound may be mutagenic.	Won, 1977
	TA100				±		
	TA1535				-		
	TA1537				-		
	TA1538				-		
Reverse mutation	S. typhimurium TA98	plate incorporation	10 µg/plate	±S9	±	NC	Wyman et al., 1979
	TA100				±		
	TA1535				+		
	TA1538				-		
Reverse mutation	S. typhimurium TA98	NR	NR	±S9	±	NC	Yoshikawa et al., 1976
Reverse mutation	S. typhimurium TA98	plate incorporation	≥5 doses/strain up to 3600 µg/plate	±S9	±	Linear dose-related increase over concentration range used for strains TA98 and TA1538 in the presence of mammalian metabolic activation.	Gocke et al., 1981
	TA100				+		
	TA1535				-		
	TA1537				-		
	TA1538				±		
Reverse mutation	S. typhimurium TA98	plate incorporation	0.1, 1 and 10 µmole/plate	None	-	NC	Chiu et al., 1978
	TA100				-		
Reverse mutation	E. coli	liquid incubation	0.010-0.018%	None	+	NC	Demerec et al., 1951
Sex-linked recessive lethal mutations	D. melanogaster	adult feeding	1.25 mM	None	+	Statistically significant ($p<0.05$) increased percentage of sex-linked recessive lethals.	Gocke et al., 1981

TABLE 5-1 (cont.)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Source
Sex-linked recessive lethal mutations	D. melanogaster	bathed eggs in aqueous solutions of compound	NR	None	-	NC	Auerbach and Robson, 1947
Sex-linked recessive lethal mutations	D. melanogaster	larval ovaries treated in vitro with compound and and then transplanted into host larvae	NR	None	-	Treatment in this manner yielded no mutations related to exposure to picric acid; however, it appears from the available abstract that a satisfactorily large experimental group was not used.	Hadorn et al., 1949
Micronucleus test for chromosome aberrations in mouse bone-marrow cells	NMRI mice of both sexes	oral gavage	2 doses at 0, 22.9, 68.7 or 91.6 mg/kg (0, 0.1, 3.0 or 0.4 mmole/kg) 2 doses at 0, 229, 343 or 458 mg/kg (0, 1.0, 1.5 or 2.0 mmole/kg)	None	-	There was no significant increase in the percentage of micronucleated polychromatic erythrocytes at any dose level tested.	Gocke et al., 1981

*Responses: +, positive; -, negative; ±, negative with and without S9 activation system; ±, positive with and negative without S9 activation system; ∓, negative with and positive without S9 activation system

NR = Not reported; NC = No comment

2,4,6-trinitrophenol, was mutagenic to tester strains TA98, TA100, TA1535 and TA1538 in the absence of a mammalian metabolic activation system. Won (1977), therefore, suggested that the metabolite rather than the parent compound may be mutagenic.

The feeding of 1.25 mM 2,4,6-trinitrophenol to adult D. melanogaster significantly ($p<0.05$) increased the incidence of sex-linked recessive lethal mutations (Gocke et al., 1981). D. melanogaster eggs bathed in a 2,4,6-trinitrophenol solution (concentration was sufficient to kill a large proportion of the eggs) did not show an increase in sex-linked recessive lethal mutations (Auerbach and Robson, 1947). Hadorn et al. (1949) also found nonsignificant mutagenic effects with the in vitro exposure of 2,4,6-trinitrophenol on larval ovaries.

2,4,6-Trinitrophenol was negative in the micronucleus test for chromosome aberrations in NMRI mouse bone-marrow cells (Gocke et al., 1981). There was no significant increase in the percentage of micronucleated polychromatic erthrocytes following oral gavage of three dose levels (229, 343 and 458 mg/kg) of 2,4,6-trinitrophenol as compared to a control. The i.p. administration of 2,4,6-trinitrophenol (22.9, 68.7 or 91.6 mg/kg) to NMRI mice also resulted in a negative micronucleus test (Gocke et al., 1981).

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of the trinitrophenol isomers were not located in the available literature.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of the trinitrophenol isomers could not be located in the available literature.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

von Oettingen (1941) summarized the studies of Gibbs and Reichert (1892) and Koizumi (1914-1915) in which rabbits and dogs, respectively, were given

repeated doses of 2,4,6-trinitrophenol. The exact duration of treatment, number of animals used and a complete description of effects were not enumerated in the available summary or abstracts. Rabbits fed repeated doses of 60 mg 2,4,6-trinitrophenol/day (duration not specified) developed jaundice, diarrhea and weight loss, while a daily dose of 180 mg 2,4,6-trinitrophenol caused severe emaciation and death within 2 weeks (Gibbs and Reichert, 1892). Unspecified kidney damage and increased nitrogen retention were observed in dogs given repeated doses (duration and route not reported) of 2,4,6-trinitrophenol at a level of 1.8 mg/kg (Koizumi, 1914-1915).

5.6. OTHER RELEVANT INFORMATION

Several other comprehensive reviews of the effects of 2,4,6-trinitrophenol include those of Howard et al. (1976), SRC (1981), U.S. EPA (1980), von Oettingen (1941) and Burrows and Dacre (1975).

The oral LD_{Lo}s for guinea pigs, rabbits and cats are reported to be 100, 120 and 250 mg/kg, respectively (NIOSH, 1983).

Kidney damage and swelling of the liver have been reported in dogs and rabbits exposed to 2,4,6-trinitrophenol (Dennie et al., 1929; von Oettingen, 1941). 2,4,6-Trinitrophenol exposure did not affect the aortic and carotid chemoreceptors of the dog (Shen, 1962), nor did it produce acute cataracts in chickens (Buschke, 1947). Furthermore, 2,4,6-trinitrophenol did not appear to induce methemoglobinemia in cats and humans(von Oettingen, 1941). 2,4,6-Trinitrophenol caused crenation of erythrocytes, an indication of expansion of the cell membranes (Sheetz and Singer, 1976).

In humans, ingestion of $\geq$1 g of 2,4,6-trinitrophenol caused acute poisoning resulting in headaches, nausea, vomiting and diarrhea (ACGIH, 1980).

Destruction of erythrocytes (anemia), gastroenteritis, hemorrhagic nephritis and acute hepatitis can develop after more chronic industrial exposure (ACGIH, 1980). Irritation to the nose, epistaxis, bronchitis and vertigo can develop after inhalation of 2,4,6-trinitrophenol dust (ITII, 1982).

Both humans and guinea pigs can be sensitized to contact with 2,4,6-trinitrophenol (Dennie et al., 1929; Maguire and Chase, 1972; Landsteiner and diSomma, 1940). The reaction is a slowly developing allergic dermatitis that can be of great intensity and can extend beyond the area of application to the skin. Weaker solutions of 2,4,6-trinitrophenol sometimes produce stronger reactions (Maguire and Chase, 1972).

Dermal exposure to this compound in the munitions industry commonly led to sensitization dermatitis (including erythema, papules, vesicles and desquamation) among workers (Schwartz, 1944).

2,4,6-Trinitrophenol inhibited liver phosphatase in dog (Sanchez and Bertran, 1950), menadione reductase and quinone reductase E. coli (Wosilait and Nason, 1954), but did not inhibit liver mitochondria phosphorylase in rats (Gladtke and Liss, 1959). 2,4,6-Trinitrophenol noncompetitively inhibited the malate dehydrogenase enzyme system in the pig heart with respect to NAD (Wedding et al., 1967).

Weinbach and Garbus (1969) reported that 2,4,6-trinitrophenol binds to mitochrondria but does not uncouple mitochondrial oxidative phosphorylation; however, 2,4,6-trinitrophenol does uncouple inside-out oriented submitochondrial particles (Hanstein and Hatefi, 1974).

At a cellular level, 2,4,6-trinitrophenol was found to increase intracellular calcium ion and potassium ion permeability in human red blood cells (Kaila and Juusela, 1982). 2,4,6-Trinitrophenol affects structural components of the cell membrane, thus affecting sodium and potassium conductances and inhibiting action potentials (Cooke et al., 1968).

6. AQUATIC TOXICITY

6.1. ACUTE EFFECTS

Early studies on the toxic effects of trinitrophenol in aquatic organisms report that the time in which minnows, Phoxinus phoxinus, lost equilibrium and turned on their sides was ~192, 237, 369, 474, 826, 1124 and 1563 minutes after exposure to 2000, 1500, 1000, 700, 400, 300 and 200 mg trinitrophenol/ℓ, respectively (Grindley, 1946). Similarly, Wilkinson (1951) reported the "over-turning time" as ~200 minutes and 24 hours, respectively, in P. phoxinus exposed to 1400 and 100 mg trinitrophenol/ℓ. Freshwater roaches, Leuciscus rutilus, were attracted to low levels of trinitrophenol (3-60 mg/ℓ), but showed signs of stress (excess surfacing and "gasping for air") at concentrations >63 mg/ℓ (Lindahl and Marcstrom, 1958).

Recently, the LC_{50} of 2,4,6-trinitrophenol was determined to be 193, 160, 164 and 167 mg/ℓ in bluegill sunfish, Lepomis macrochirus, exposed for 24, 48, 72 and 96 hours, respectively (U.S. EPA, 1978; Buccafusco et al., 1981). The no-effect concentration for 96 hours exposure was reported to be <77 mg/ℓ for this species (U.S. EPA, 1978). In the marine sheepshead minnow, Cyprinodon variegatus, the 24-, 48-, 72- and 96-hour LC_{50} values were each reported to be 134 mg/ℓ, while the no-effect concentration was determined to be 100 mg/ℓ (U.S. EPA, 1978; Heitmuller et al., 1981).

The 24- and 48-hour LC_{50} values for the freshwater crustacean, Daphnia magna, exposed to 2,4,6-trinitrophenol were >220 and 84.7 mg/ℓ, respectively (U.S. EPA, 1978; LeBlanc, 1980). The 48-hour no-effect concentration was determined to be <28 mg/ℓ. Bringmann and Kuhn (1977) determined a 24-hour LC_{50} value of 145 mg/ℓ for D. magna. The LC_{50} values for the mysid shrimp, Mysidopsis bahia, following 48-, 72- and 96-hour exposures

were 56.0, 36.0 and 19.7 mg/ℓ, respectively (U.S. EPA, 1978). The 96-hour no-effect concentration for M. bahia was 5.6 mg/ℓ.

6.2. CHRONIC EFFECTS

Pertinent data regarding the effects of chronic exposure to trinitrophenol on aquatic organisms could not be located in the available literature.

6.3. PLANT EFFECTS

Palmer and Maloney (1955) reported that trinitrophenol tested at 2 mg/ℓ for exposures of 3, 7, 14 and 21 days was not toxic for any duration in blue-green algae (Cylindrospermum licheniforme and Microcystis aeruginosa), green algae (Chlorella variegata and Scenedesmus obliquus), or diatoms (Gomphonema parvulum and Nitzschia palea). In the green alga, Scenedesmus. and the blue-green alga, Microcystis aeruginosa, the toxicity threshold levels, or levels causing the onset of cell multiplication inhibition, were 61 and 40 mg 2,4,6-trinitrophenol/ℓ, respectively, after 8 days exposure (Bringmann and Kuhn, 1978). In 96-hour exposures with the saltwater alga, Skeletonema costatum, concentrations of 2,4,6-trinitrophenol causing 50% reduction of chlorophyll a and cell number were 62.7 and 141 mg/ℓ, respectively (U.S. EPA, 1978).

6.4. RESIDUE

Pertinent data regarding residues of trinitrophenols in aquatic organisms could not be located in the available literature. However, based on its water solubility and octanol-water partition coefficient, and the regression equations of Kenaga and Goring (1980), a BCF of 3 is predicted for 2,4,6-trinitrophenol, indicating virtually no potential for bioaccumulation.

6.5. OTHER RELEVANT INFORMATION

Activation (fertilization) of eggs of the marine polychaete worm, Nereis limbata, was inhibited by 230 mg trinitrophenol/ℓ (LeFevre, 1945, 1948).

7. EXISTING GUIDELINES AND STANDARDS

7.1 HUMAN

The TLV-TWA for 2,4,6-trinitrophenol, recommended by ACGIH (1980) and adopted by OSHA (1981), is 0.1 mg/m³. ACGIH (1980) has recommended a STEL of 0.3 mg/m³ for 2,4,6-trinitrophenol. Both sources have noted that there may be a significant potential contribution to the overall exposure by the dermal route.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of trinitrophenols were not located in the available literature.

8. RISK ASSESSMENT

2,4,6-Trinitrophenol was negative in a carcinogenicity assay with Wistar rats, in which both sexes of animals were fed a dietary concentration of 500 ppm of 2,4,6-trinitrophenol for 2.5 years (van Esch et al., 1957). The evidence from this study is not conclusive because the incidence of mammary tumors in the control Wistar animals (8/19; 42%) was higher than usually observed (18/83; 22%), and the number of animals/group was small (10 treated and 19 controls). There is some evidence that 2,4,6-trinitrophenol is mutagenic. 2,4,6-Trinitrophenol tested positive in the reverse mutation assay with Salmonella typhimurium only in the presence of a mammalian metabolic activation system (Won, 1977; Wyman et al., 1979; Yoshikawa et al., 1976; Gocke et al., 1981; Chiu et al., 1978). A statistically significant ($p<0.05$) incidence of sex-linked recessive lethal mutations was induced in Drosophila melanogaster by feeding adults a 1.25 mM solution of 2,4,6-trinitrophenol (Gocke et al., 1981). Studies regarding the potential teratogenicity of this isomer were not located in the literature searched.

Chronic toxicity studies with 2,4,6-trinitrophenol were not located in the literature searched. Two studies from the early literature appear to be subchronic in nature. Rabbits given repeated doses of 60 mg 2,4,6-trinitrophenol/day developed jaundice, diarrhea and weight loss (Gibbs and Reichert, 1892), while unspecified kidney damage and increased nitrogen retention were observed in dogs given repeated doses of 2,4,6-trinitrophenol at a level of 1.8 mg/kg (Koizumi, 1914-1915). Because these levels of exposure produced frank toxic effects, and because of the lack of information regarding the duration of treatment and number of animals used, and lack of a complete description of effects, neither of these two studies can be used for derivation of an ADI for 2,4,6-trinitrophenol. No other subchronic studies were located in the available literature.

Lack of carcinogenicity and chronic toxicity data also precludes quantitative risk assessment for the other trinitrophenol isomers.

9. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. 486 p.

Auerbach, C. and J.M. Robson. 1947. XXXIII. Tests of chemical substances for mutagenic action. Royal Soc. Edinburgh Proc., Sec. B (Biology). 62(3): 284-291.

Barral, E. 1915. Picric acid and malingering. Soc. Biol. p. 453; J. Pharm. Chim. 12: 228-229.

Brebion, G., R. Cabridenc and B. Huriet. 1967. Studying the biodegradation possibilities of industrial effluents. Application to the biodegradation of phenols. Rev. Inst. Fr. Pet. Ann. Combust. Liq. 22(6): 1029-1052.

Bringmann, G. and R. Kuhn. 1959. The toxic effects of waste water on aquatic bacteria, algae and small crustaceans. Gesundbeits-Ing. 80: 115. (Cited in McKee and Wolf, 1963)

Bruin, P., G.J. Bergen and J.J. Desta, Ed. 1980. Handling Chemicals Safely, 2nd ed. Dutch Assoc. of Safety Experts, Dutch Chemical Industry Assoc., and Dutch Safety Institute, the Netherlands. 1013 p.

Buccafusco, R.J., S.J. Ells and G.A. LeBlanc. 1981. Acute toxicity of priority pollutants to bluegill Lepomis macrochirus. Bull. Environ. Contam. Toxicol. 26(4): 446-452.

Burrows, D. and J.C. Dacre. 1975. Toxicity to aquatic organisms and chemistry of nine selected waterborne pollutants from munitions manufacture. Literature evaluation. NTIS AD-A Rep. 96 p.

Buschke, W. 1947. Acute reversible cataract in chicken due to various nitrocompounds. Am. J. Ophthamol. 30: 1356-1368.

Chambers, C.W., H.H. Tabak and P.W. Kabler. 1963. Degradation of aromatic compounds by phenol-adapted bacteria. J. Water Pollut. Control Fed. 35: 1517-1528.

Chiu, C.W., L.H. Lee, C.Y. Wang and G.T. Bryan. 1978. Mutagenicity of some commercially available nitro compounds for Salmonella typhimurium. Mutat. Res. 58(1): 11-22.

Cole, J.A., Ed. 1974. Groundwater Pollution in Europe. Proc. Conf. (Cited in U.S. EPA, 1980)

Cooke, I.M., J.M. Diamond, A.D. Grinnell, S. Hagiwara and H. Sakata. 1968. Suppression of the action potentials in nerve by nitrobenzene derivatives. Proc. Natl. Acad. Sci. 60(2): 470-477.

Demerec, M., G. Bertani and J. Flint. 1951. A survey of chemicals for mutagenic action on E. coli. Am. Nat. 85: 119-136.

Dennie, C.C., W.L. McBride and P.E. Davis. 1929. Toxic reactions produced by the application of trinitrophenol (picric acid). Arch. Dermatol. Syphilology. 20: 698-704.

Gibbs, W. and E.T. Reichert. 1892. Systemic study of the action of constitutionally related chemical compounds on the animal organisms. Arch. Anat. Physiol. Suppl. p. 259. (Cited in von Oettingen, 1941)

Giorgi, G. 1924. Reduction of picric acid in the liver, kidney and spleen. Policlinico Sez. Med. 31: 184-188. (CA 19: 3106)

Gladtke, E. and E. Liss. 1959. Influence on oxidative phosphorylation of rat liver mitochondria of various nitrophenols. Biochem. Z. 331: 65-70.

Gocke, E., M.T. King, K. Eckhardt and D. Wild. 1981. Mutagenicity of cosmetics ingredients licensed by the European communities. Mutat. Res. 90(2): 91-109.

Gold, V. and C.H. Rochester. 1964. Reactions of aromatic nitro compounds in alkaline media. IV. Photochemical reactions in methanolic sodium methoxide solutions. J. Chem. Soc. p. 1704-1710. (CA 64: 557d)

Goodwin, A.E., D.K. Cabbiness and H.A. Mottola. 1977. Some rate considerations on COD determinations. Water Air Soil Pollut. 8(4): 467-478.

Grindley, J. 1946. Toxicity to rainbow trout and minnows of some substances known to be present in waste water discharges to rivers. Ann. Appl. Biol. 33: 103.

Guerbet, M. and A. Mayer. 1932. Pharmacodynamic action of nitrated phenols. An agent increasing cellular oxidations, 2,4-dinitrophenol. V. Presence of 2,4-dinitrophenol and its derivatives in the organs and liquids of the body during intoxication. Elimination by the urine. Ann. Physiol. Physicochim. Biol. 8: 117-121. (CA 26: 5652)

Gundersen, K. and J.L. Jensen. 1956. Soil bacterium decomposing organic nitro compounds. Acta. Agric. Scand. 6: 100-114. (CA 50: 10958b)

Gvozdyak, P.I., N.F. Mogilevich and M.N. Rotmistrov. 1974. Reduction of trinitrophenol by denitrifying bacteria. Mikrobiol. Zh. 36(4): 424-428. (Ukr.) [CA 82(11): 70182c]

Hadorn, E., S. Rosin and G. Bertani. 1949. Results of mutation studies with chemical treatment of Drosophila ovaries in vitro. Hereditas. p. 256-266. (Ger.) (CA 45: 5832e)

Hansch, C. and A. Leo. 1979. Substituent Constants for Correlation Analysis in Chemistry and Biology. Wiley-Interscience, New York, NY.

Hanstein, W.G. and Y. Hatefi. 1974. Trinitrophenol: A membrane-impermeable uncoupler of oxidative phosphorylation. Proc. Natl. Acad. Sci. 71: 288-292.

Harris, A.H., O.F. Binkley and B.M. Chenoweth, Jr. 1946. Hematuria due to picric acid poisoning at a Naval anchorage in Japan. Am. J. Public Health. 36: 727.

Hawley, G.G., Ed. 1977. The Condensed Chemical Dictionary, 9th ed. Van Nostrand Reinhold Company, NY. p. 312, 618.

Heitmuller, P.T., T.A. Hollister and P.R. Parrish. 1981. Acute toxicity of 54 industrial chemicals to sheepshead minnows (Cyprinodon variegatus). Bull. Environ. Contam. Toxicol. 27(5): 596-604.

Howard, P.H., J. Santodonato, J. Saxena, J. Malling and D. Greninger. 1976. Investigation of selected potential environmental contaminants: Nitroaromatics. Prepared for OTS, U.S. EPA, Washington, DC under Contract No. 68-01-2999. EPA 560/2-76-010.

ITII (International Technical Information Institute). 1982. Toxic and hazardous industrial chemicals safety manual for handling and disposal with toxicity and hazard data. ITII, Tokyo, Japan. 700 p.

Jensen, H.L. and G. Lautrup-Larsen. 1967. Microorganisms that decompose nitro-aromatic compounds, with special reference to dinitro-o-cresol. (Cited in Howard et al., 1976)

Kaila, K. and A. Juusela. 1982. Calcium-dependent increase in the potassium permeability of human red blood cells by pentachlorophenol and 2,4,6-trinitrophenol. Med. Biol. 60(5): 260-266.

Karplus, J.P. 1893. No title provided. Z. Klin. Med. 22: 210. (Cited in von Oettingen, 1941)

Kenaga, E.E. and C.A.I. Goring. 1980. Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota. In: Aquatic Toxicology, ASTM STP 707, J.G. Eaton, P.R. Parrish and A.C. Hendrics, Ed. Am. Soc. Test. Mater., Philadelphia, PA. p. 78-115.

Koizumi, T. 1914-1915. On poisoning with picric acid used in industry. Zentr. Biochem. Biophys. 17: 615. (Cited in von Oettingen, 1941)

Landsteiner, K. and A.A. diSomma. 1940. Studies on the sensitization of animals with simple chemical compounds. VIII. Sensitization to picric acid; subsidiary agents and modes of sensitization. J. Exp. Med. 72: 361. (Cited in Maguire and Chase, 1972)

LeBlanc, G.A. 1980. Acute toxicity of priority pollutants to water flea (Daphnia magna). Bull. Environ. Contam. Toxicol. 24(5): 684-691.

LeFevre, P.G. 1945. Certain chemical factors influencing artificial activation of Nereis eggs. Biol. Bull. 89: 144-156.

LeFevre, P.G. 1948. Further chemical aspects of the sensitization and activation reactions of Nereis eggs. Biol. Bull. 95: 333-345.

Lindahl, P.E. and A. Marcstrom. 1958. On the preference of roaches, Leuciscus rutilas, for trinitrophenol, studied with the Fluviarium technique. J. Fish Res. 15(4): 685-694.

Maguire, H.C. and M.W. Chase. 1972. Studies on the sensitization of animals with simple chemical compounds. XIII. Sensitization of guinea pigs with picric acid. J. Expt. Med. 135: 357-375.

Malmejac, F. 1917. Picric acid jaundice and true icterus. J. Am. Med. Assoc. 68: 923.

Matsugma, H.J. 1967. Nitrophenols. In: Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 2, 2nd ed., A. Standen, Ed. John Wiley and Sons, Inc., NY. p. 888-894.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. State Water Qual. Control Board, the Resources Agency of California. Publ. No. 3-A. (Cited in U.S. EPA/NIH, 1983)

NIOSH (National Institute for Occupational Safetyand Health). 1983. RTECS (Registry of Toxic Effects of Chemical Substances). Online: May, 1983.

Nose, K., T. Suzuki and K. Fukunaga. 1964. Adsorption of phenols on fuller's earth. Nipon Dojo-Hiryogaku Zasshi. 35(2): 57-60. (Jap.) (CA 62: 53c)

OSHA (Occupational Safety and Health Administration). 1981. General Industry Standards. OSHA Safety and Health Standards reprinted from 29 CFR 1910. U.S. Dept. Labor. p. 635.

Palmer, C.M. and T.E. Maloney. 1955. Preliminary screening for potential algicides. Ohio J. Sci. 55(1): 1-8.

Pitter, P. 1976. Determination of biological degradability of organic substances. Water Res. 10: 231-235.

Pitter, P., R. Palyza and K. Hubnerova-Hajkova. 1974. Relation between the structure and biodegradability of organic compounds. V. Biodegradability of aromatic nitroderivatives. Sb. Vys. Sk. Chem.-Technol. 19: 77-98. (Cze.) [CA 85(6): 36913u]

Rutledge, L.J. 1936. Toxic nephritis following the use of picric acid as a nasal spray. J. Am. Med. Assoc. 107: 1322.

Ryerman, D.W., A.V.S. Prabhakara Rho and J.C. Buzzell, Jr. 1966. Behavior of organic chemicals in the aquatic environment. Manufacturing Chemists Association, Washington, DC. (Cited in U.S. EPA/NIH, 1983)

Sanchez, F.S. and E.C. Bertran. 1950. Action of some organic compounds on acid phosphomonoesterase of dog liver. Anales facultad vet. univ. Madrid y Inst. Invest. Vet. 2: 70-78.

Schwartz, L. 1944. Dermatitis for explosives. J. Am. Med. Assoc. 125: 186.

Sheetz, M.P. and S.J. Singer. 1976. Equilibrium and kinetic effects of drugs on the shapes of human erythrocytes. J. Cell Biol. 70: 247-251.

Shen, T.C.R. 1962. The stimulating effect of dinitro-o-cresol, dinitrophenol and p-nitrophenol on the aortic chemoreceptors in dogs. Arch. Intern. Pharmacodyn. 140: 521-527. (Cited in SRC, 1981)

SRC (Syracuse Research Corporation). 1981. Information Profiles on Potential Occupational Hazards: Nitrophenols. Prepared by the Center for Chemical Hazard Assessment, Syracuse Research Corporation, Syracuse, NY, for NIOSH, Rockville, MD under Contract No. 210-79-0030.

Tsukamura, M. 1954a. The enzymatic reduction of picric acid. Igaku to Seibutsugaku. 33: 59-62. (CA 50: 101526)

Tsukamura, M. 1954b. Mechanism of the enzymic reduction of picric acid. Igaku to Seibutsugaku. 33: 270-273. (CA 50: 10152e)

Tsukamura, M. 1960. Enzymatic reductions of picric acid. J. Biochem. 48: 662-671. (Cited in Wyman et al., 1979) (CA 55: 65931)

U.S. EPA. 1978. In-depth studies on health and environmental impacts of selected water pollutants. Unpublished progress report. Prepared by Syracuse Research Corporation under Contract 68-01-4646.

U.S. EPA. 1980. Ambient Water Quality Criteria for Nitrophenols. Environmental Criteria and Assessment Office, Cincinnati, OH. EPA 440/5-80-063. NTIS PB 81-117749.

U.S. EPA. 1983. TSCA Inventory (Toxic Substances Control Act). Online: May, 1983.

U.S. EPA/NIH (National Institute of Health). 1983. OHM-TADS (Oil and Hazardous Materials Technical Assistance Data System). Online: May, 1983.

van Esch, G.J., H.H. Vink and H. van Genderen. 1957. Influence of hexanitrodiphenylamine on the incidence of neoplasms in the mammary tissue of rats. Nature. 180(4584): 509-510.

von Oettingen. 1941. X. Trinitrophenol (picric acid). In: The Aromatic Amino and Nitro Compounds, Their Toxicity and Potential Dangers, A Review of the Literaure. Pub. Health Bull. No. 271. p. 149-155. Federal Security Agency, PHS, Washington, DC.

Walko, K. 1901. No title provided. Arch. Exp. Path. Pharmak. 46: 181. (Cited in von Oettingen, 1941; Williams, 1959)

Wedding, R.T., C. Hansch and T.R. Fukuto. 1967. Inhibition of malate dehydrogenase by phenols and the influence of ring substituents on their inhibitory effectiveness. Arch. Biochem. Biophys. 121: 9-21.

Weinbach, E.C. and J. Garbus. 1969. Mechanism of action of reagents that uncouple oxidative phosphorylation. Nature. 221: 1016-1018.

Wilkinson, R. 1951. Treatment and disposal of waste waters containing picric acid and dinitrophenol. Ind. Chem. Jan.-Feb., 1951. (Cited in McKee and Wolf, 1963; Burrows and Dacre, 1975)

Williams, T.C. 1959. Detoxication Mechanisms. John Wiley and Sons, Inc., New York, NY. p. 420-423.

Windholz, M., Ed. 1976. The Merck Index, An Encyclopedia of Chemicals and Drugs, 9th ed. Merck and Co., Inc., Rahway, NJ. p. 7208.

Won, W.D. 1977. Picric acid and its biodegradation products as mutagens. Abstr. Annu. Meet. Am. Soc. Microbiol. 77: 276.

Wosilait, W.D. and A. Nason. 1954. Pyridine nucleotide-menadione reductase from E. coli. J. Biol. Chem. 208: 785-798.

Wyman, J.R., H.E. Guard, W.D. Won and J.H. Quay. 1979. Conversion of 2,4,6-trinitrophenol to a mutagen by Pseudomonas aeruginosa. Appl. Environ. Microbiol. 37(2): 222-226.

Yoshikawa, K., H. Uchino and H. Kurata. 1976. Studies on the mutagenicity of hair dyes. Bull. Natl. Inst. Hyg. Sci. (Toyko). 94: 28-32. (Jap.) (CA 88: 164999a)

APPENDIX: LITERATURE SEARCHED

With the exception of a few physical and chemical properties, no data were found for 2,3,4-, 2,3,5-, 2,3,6- and 3,4,5-trinitrophenol. Therefore, this profile contains data almost exclusively for 2,4,6-trinitrophenol. Some of these data were taken in whole or in part from the review documents of 2,4,6-trinitrophenol prepared by SRC (1981) and Howard et al. (1976).

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
EPCASR
Chemical Industry Notes

Most of these searches were conducted in February, 1983; a few were conducted March-May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 7 and 8th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. 486 p.

ACGIH (American Conference of Governmental Industrial Hygienists). 1982. Documentation of the Threshold Limit Values for Chemical Substances in Work Air. Cincinnati, OH. 94 p.

Bruin, P., G.J. Bergen and J.J. Desta, Ed. 1980. Handling Chemicals Safely, 2nd ed. Dutch Assoc. of Safety Experts, Dutch Chemical Industry Assoc., and Dutch Safety Institute, The Netherlands. 1013 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, Vol. 2A, 3rd rev. ed. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, Vol. 2B, 3rd rev. ed. John Wiley and Sons, NY. 2879-3816 p.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, Vol. 2C, 3rd rev. ed. John Wiley and Sons, NY. 3817-5112 p.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. 575 p.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

Muir, G.D., Ed. 1977. Hazards in the Chemical Laboratory, 2nd ed. The London Chemical Society, London. 473 p.

NTP (National Toxicology Program). 1983. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status. April 20, 1983.

Proctor, N.H. and J. P. Hughes. 1978. Chemical Hazards of the Workplace. J.B. Lippincott Co., Philadelphia, PA. 533 p.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.